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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	

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32

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)
Office Action Summary	08/978,636	RABBBANI ET AL.
	Examiner	**Art Unit**
	Mary M. Schmidt	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *245-260* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *245-260* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 1997* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1 ☐ Certified copies of the priority documents have been received.

2 ☐ Certified copies of the priority documents have been received in Application No. _____ .

3 ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Note that the election of species requirement in the paper mailed 12/6/02 is withdrawn.

Claims 245-260 are pending.

Drawings

2. The drawings dated 11-25-97 are objected to and corrections are required according to the PTO-948 mailed with the previous Office action on 12/03/02.

Claim Objections

3. Claim 249 has a typographical error in line 3. The "reverese" needs to be replaced with "reverse".

Claim Rejections - 35 USC § 112

4. Claims 245-260 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 245 is drawn to a nucleic acid construct which when introduced into a cell codes for and expresses a non-native polymerase, said polymerase being capable of producing more than one copy of a nucleic acid sequence from said construct, wherein said polymerase is

expressed solely in a eukaryotic cell. Claim 246 states the construct of claim 245, further comprising a recognition site for said non-native polymerase. Claim 247 states the construct of claim 246, wherein said recognition site is complementary to a primer for said non-native polymerase. Claim 248 states the construct of claim 247, wherein said primer comprises transfer RNA (tRNA). Claim 249 states the construct of claim 245, wherein said non-native polymerase comprises a member selected from the group consisting of DNA polymerase, RNA polymerase, reverse transcriptase, and a combination thereof. Claim 250 states the construct of claim 249, wherein said RNA polymerase comprises a bacteriophage RNA polymerase. Claim 251 states that the construct of claim 250, wherein said bacteriophage RNA polymerase is selected from the group consisting of T3, T7, SP6 and a combination thereof. Claim 252 states the construct of claim 249, further comprising a promoter for said RNA polymerase. Claim 253 states wherein the nucleic acid produced from said construct (in claim 245) is selected from the group consisting of DNA, RNA, a DNA-RNA hybrid, a DNA-RNA chimera and a combination of the foregoing. Claim 254 states wherein the DNA or RNA comprises sense or antisense or both.

Claim 255 is drawn to a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing. Claim 256 states the processing element comprises an RNA processing element. Claim 257 is drawn to the construct of claim 256, wherein said RNA processing element is selected from the group consisting of an intron, a polyadenylation signal, a capping element, and a combination of the

foregoing. Claim 258 states that the nucleic acid product is single stranded. Claim 259 is drawn to the construct of claim 255, wherein said nucleic acid product is selected from the group consisting of antisense RNA, antisense DNA, sense RNA, sense DNA, a ribozyme, a protein binding nucleic acid sequence, and a combination of the foregoing. Claim 260 is drawn to the construct of claim 259, wherein said protein binding nucleic acid sequence comprises a decoy that binds a protein required for viral assembly or viral replication.

The specification teaches several constructs designed for entry into a cell and expression of one or more sequences to perform a biological function such as antisense inhibition of a nucleic acid. Specifically, several CHENAC constructs are taught prophetically, and pictured in figures 1-13 as vector based constructs constructed by using modified nucleic acid regions and designed to provide improved entry into a cell by way of improved construct-cell interaction. A second group of nucleic acid fused with antibody based constructs are taught prophetically and shown in figures 14-21. Preparation of multimeric insulin by means of nucleic acid hybridization is further taught prophetically and shown in figures 22-23. No exemplification for such constructs is taught in the specification as filed.

By way of specific design and example, vectors for antisense inhibition of HIV in cells by co-expression of antisense DNA under control of a T7 promoter with a T7 polymerase (represented in figures 24-49) are taught and supported by *in vitro* data in the specification as filed. Specifically, construction of the M13 phage vectors pRT-A, pRT-B, and pRT-c are taught which contain the coding sequence for the T7 RNA polymerase driven by the RSV promoter and

with an SV40 intron sequence that will be spliced out to form a functional polymerase enzyme and each respective construct also having the antisense A, B, and C sequences driven by a T7 promoter and terminated by a T7 terminator. A modified version of the pINT-3 construct (the parent vector of pRT-A, B and C vectors before insertion of the antisense sequences) is taught where a polylinker is inserted behind the poly-A tail of the T7 polymerase gene for subsequent sub-cloning of the lacZ gene in this instance to form pINT-LacZ. The result upon introduction in a eukaryotic cell would be synthesis of the T7 polymerase from the RSV promoter which in turn acts upon the T7 promoter to synthesize B-galactosidase.

Furthermore, plasmids are taught containing anti-sense segments introduced into the transcript region of the U1 gene, plasmid pHSD-4 U1 so that upon expression of the transcript, the antisense RNA sequence is produced to the complementary region of the HIV genome. Specifically, pDU1-A, B, C and D were made using the antisense A, B, and C sequences previously described and D as a control containing a non-HIV sequence. A multi-cassette version of the constructs was also made by sub-cloning in tandem the A,B, and C antisense to make pNDU1 (A,B,C) (N meaning the construct was also contained the gene for neomycin resistance).

Other multi-cassette constructs taught were:

(1) TRI 101, an M13 phage vector containing the "A" antisense T7 operon , the "B" antisense T7 operon and the "C" antisense T7 operon in a single construct (figure 46). Co-transfection would be required for expression of the antisense molecules from this construct with

a vector that expresses T7 RNA polymerase (suggested is the intron containing construct of example 19); and,

(2) an M13 construct constructed from a multi-ligation of portions of pINT-3 (containing the intron containing polymerase) and the T7 promoter driven A, B, and C sequences (see figure 47).

The specification teaches application of some of these constructs ("various U1 constructs described above" p. 167, last line) in antisense inhibition of HIV in infected U937 cell culture. Specifically the following is shown: (1) expression of A, B, and C antisense by hybridization analysis after expression of the "U1 clone" (p. 169, line 3), (2) expression of the "triple U1 construct" (p. 169, para. (c), line 1) which result in a decrease in p24 production next to the control, and increased % reduction in p24 over time and after re-infection of cells, and these results were confirmed by absence p24 amplification next to control cells via PCR of the targeted DNA, and (3) expression of the construct of figure 50, a fusion product antisense A upstream of B-gal gene where antisense activity of the A portion caused inhibition of B-gal activity as shown in lacZ assays. The results in figure 51 show HIV A/Anti-A activity and HIV A/Anti-ABC (when the triple U1 construct was used by *co-transfection*) as the equivalent of the uninfected cells whereas the infected and control containing cells showed high B-gal expression. Therefore, it does not appear in the specification as filed that the multicassette A,B,C and T7 polymerase construct (expressed on same plasmid) was applied to the same HIV challenge experiments.

Additional constructs are more prophetically taught: the primary nucleic acid construct that propagates production centers for the production of single-stranded antisense, etc. in examples 21-25, and the retrovirus vector containing sequences for the expression of antisense RNA directed at HIV on page 181, last para.

MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art at the time the invention was made:

> The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence....A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process....Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement....The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

The instantly claimed compositions are considered to lack written description in the specification as filed for a representative number of species of any possible nucleic acid construct which when introduced into a cell codes for and expresses a non-native polymerase which is

capable of producing more than one copy of a nucleic acid sequence from said construct and wherein said polymerase is expressed solely in a eukaryotic cell because the text of the specification as filed provides only general guidance, and not specific guidance, for the design and use of the claimed compounds. The U1-antisense compounds summarized above have a T7 RNA polymerase promoter from which the U1-antisense are expressed, however, no actual expression of a non-native polymerase is taught in a eukaryotic cell in the specification as filed. On page 82 of the specification, applicants teach the following:

> Among the significant embodiments is a nucleic acid construct which when introduced into a cell expresses a non native polymerase, the polymerase being capable of producing more than one copy of a nucleic acid sequence from the construct. This construct can further comprise a recognition site for the non native polymerase. Such a recognition site can be complementary to a primer for the non native polymerase. The primer preferably comprises transfer RNA (tRNA).
>
> In certain embodiments the non native polymerase comprises a member selected from DNA polymerase, RNA polymerase and reverse transcriptase as well as any combination of the foregoing enzymes. The RNA polymerase preferably comprises a bacteriophage RNA polymerase, e.g., T3, T7, and SP6, or combinations thereof. Furthermore, the above-described construct can comprise a promoter for the RNA polymerase.

Thus, from the description in the specification, it appears that the invention contemplates expressing, for example, an RNA polymerase from any nucleic acid construct such as a vector. The specification further states that it is expressed from a plasmid construct which also has a recognition (binding site, such as a promoter site) that recognizes the polymerase. Other than this general description of using any nucleic acid construct with any such polymerase, there is no further reduction to practice in the specification as filed. Considering the nebulous breadth of

claim 245 where any possible nucleic acid which when introduced into a cell codes for and expresses a non-native polymerase, one of skill in the art would not have been able to readily visualize a representative number of species of such a broad genus. The claimed genus could comprise any type of vector construct, the correlation between structure and function, especially for functions in cells in a whole organism, are not readily apparent for the specification as filed. The reference in the specification to RNA polymerases such as T3, T7, SP6 or reverse transcriptase generally, does not provide a specific nexus between structure of such polymerases expressed from any possible nucleic acid construct and functions thereof in any eukaryotic cell. Thus, in view of the substantial variation among the species of any possible nucleic acid construct expressing any possible polymerase in a eukaryotic cell, one of skill in the art would not have recognized that there were a representative number of species implicitly or explicitly disclosed in the specification as filed or that applicant was in possession of the necessary common attributes or features of any such nucleic acid construct for the breath of the genus claimed. Thus, one of skill in the art would not have recognized that application was in possession of a representative number of species of the claimed nucleic acid constructs.

Response to Arguments

5. Applicant's arguments filed 06/18/2002 have been fully considered but they are not persuasive.

On pages 9 and 10 of the response filed 6/18/02, applicants "assert that adequate description has been provided. A detailed description of the constructs for producing products in accordance with the present invention is described throughout the specification. Although vector type constructs for producing desirable products are the preferred embodiment of the present invention, Applicants respectfully submit that their claimed invention should not be so limited, particularly on an issue of written description. Sufficient identifying characteristics of the Applicants' claimed constructs for producing products is provided as noted above in the specification. Lastly, Applicants note that actual reduction to practice is not required to satisfy the Written Description Requirement"

In response, although actual reduction to practice is not required to adequately describe the claimed invention, one of skill in the art must be able to readily envisage both the breath of the genus of claimed constructs as well as the representative number of species of any such genus of constructs as defined by certain common attributes and features. In the instant case, the constructs are nucleic acid constructs which when present in a cell produce a polymerase product as well as other possible products. The genus the involves production of a product in a cell. Not all cells are alike, and the environmental conditions alter drastically from use of cells in cell culture to use of cells in a whole organism which are intimately connected to other cells in the whole organism. Thus, the genus of cells in which the nucleic acid constructs are expressed is critical to understanding the genus of the claimed constructs since the claims have the function limitation that the nucleic acid construct is introduced into a cell and codes for and expresses a

non-native polymerase. Additionally, to understand the breath of the claimed genus, one of skill in the art must consider the breath of the nucleic acid constructs claimed. Typically in the art, only a vector-type construct is capable of having the function of coding for and expressing a protein from the encoding nucleic acid gene sequence. Since nucleic acid constructs are composed of nucleic acids, having a defined sequence of bases, one of skill in the art would not readily envisage any such nucleic acid construct absent the nucleic acid sequence of said construct. This is true also for the polymerase expressed from the nucleic acid construct. Thus, the claimed genus is extremely broad since it is drawn to any possible nucleic acid construct expressing a polymerase in a cell. And since the specification as filed does not further provide the essential material of defining the common elements of nucleic acid sequence structure of any such nucleic acid composition, one of skill in the art does not have a clear vision of a representative number of species of any such nucleic acid construct. The invention should be clearly defined in the specification as filed and essential material to the claimed invention (such as the nucleic acid sequences of the claimed nucleic acid constructs) can only be incorporated by reference to a patent publication (see MPEP 608.01(p)(A)). Thus, the claims are not adequately described by the specification as filed for the breath of claimed constructs.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 245-247 and 249-254 are rejected under 35 U.S.C. 102(e) as being anticipated by Wagner et al. (U.S. Patent 5,591,601), for the same reasons of record as set forth in the Official action mailed 02/18/99,11/10/99, 12/19/00 and 12/06/02.

Claim 245 is drawn to a nucleic acid construct which when introduced into a cell codes for and expresses a non-native polymerase, said polymerase being capable of producing more than one copy of a nucleic acid sequence from said construct, wherein said polymerase is expressed solely in a eukaryotic cell. Claim 246 states the construct of claim 245, further comprising a recognition site for said non-native polymerase. Claim 247 states the construct of claim 246, wherein said recognition site is complementary to a primer for said non-native polymerase. Claim 249 states that the non-native polymerase comprises a member selected from the group consisting of DNA polymerase, RNA polymerase, reverse transcriptase, and a combination thereof. Claim 250 states that the RNA polymerase comprises a bacteriophage

RNA polymerase. Claim 251 states the bacteriophage RNA polymerase is selected from the group consisting of T3, T7, SP6 and a combination thereof. Claim 252 states that the construct further comprises a promoter for said RNA polymerase. Claim 253 states wherein the nucleic acid produced from said construct (in claim 245) is an RNA. Claim 254 states wherein the RNA is an antisense.

Wagner et al. taught in col. 2, line 46, through col. 3, line 2:

> The present invention is based, in part on Applicants' discovery of significant gene expression from a DNA construct complexed to T7 RNAP, which construct contains a T7 RNAP gene driven by a T7 promoter, and another nucleotide sequence encoding a functional or a reporter gene i.e. a gene of interest, under the control of a second T7 promoter (T7T7/T7-gene construct). One unique feature of the construct which distinguishes this system from other gene expression systems is that both the initiation and maintenance of gene expression depend upon the binding of T7 RNAP to DNA prior to the introduction of the construct into host cells. The complex of prebound RNAP to plasmid DNA is stable without detachment during entry into cells. Once the DNA-RNAP enzyme complex enters the cytoplasm of the cells, transcription is initiated immediately by the plasmid. The subsequent production of T7 RNAP enzyme, in turn, triggers transcription of the functional/reporter gene as well as continued synthesis of additional T7 RNAP, thus it is both a self-initiating and self-sustaining system. The transcription of both the T7 RNAP and the functional/reporter genes can be driven repeatedly by newly synthesized T7 RNAP in the cell cytoplasm without nuclear integration.

In col. 5, lines 8-9, they further teach that this system is used in eukaryotic cells. In col. 6, lines 65-67, and col. 7, lines 1-5, they teach that "[a]lso within the scope of the invention is the expression of oligo-ribonucleotide sequences, that include anti-sense RNA and ribozymes that function to inhibit the translation of a variety of mRNA. Anti-sense RNA acts to directly block

the translation of mRNA by binding to targeted mRNA and preventing protein translation, either by inhibition of ribosome binding and/or translocation or by bringing about the nuclease degradation of the mRNA molecule itself."

See also col. 7, line 45, through col. 8, line 14, where they describe their "autogene" system as used in "the intended eukaryotic host cell" (col. 7, lines 64-65) and that "[e]xamples of RNA polymerases suitable for use in the present invention include, but are not limited to, the RNA polymerases of the T7, T3, SP6, or K11 bacteriophages of the RNA polymerases of mitochondria." (Col. 8, lines 9-12)

8. Claim 245 is rejected under 35 U.S.C. 102(b) as being anticipated by Fuerst et al. (PNAS, Vol. 83, pp. 8122-8126, 1986).

Claim 245 is drawn to a nucleic acid construct which when introduced into a cell codes for and expresses a non-native polymerase, said polymerase being capable of producing more than one copy of a nucleic acid sequence from said construct, wherein said polymerase is expressed solely in a eukaryotic cell.

Fuerst et al. taught expression of a bacteriophage T7 RNA polymerase in eukaryotic human TK- 143 and HeLa cells (see page 8122, col. 2, "virus and cells" and figure 1 on page 8123 for description of the recombinant virus with T7 polymerase used to infect the eukaryotic cells.

9. Claims 255-259 are rejected under 35 U.S.C. 102(b) as being anticipated by De Young et al. (Biochemistry, 1994, Vol. 33, No. 40, pp. 12127-12138).

Claim 255 is drawn to a nucleic acid construct which when introduced into a cell produces a product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing. Claim 256 is drawn to the construct of claim 255, wherein said processing element comprises an RNA processing element. Claim 257 is drawn to the construct of claim 256, wherein said RNA processing element is selected from the group consisting of an intron, a polyadenylation signal, a capping element, and a combination of the foregoing. Claim 258 is drawn to the construct of claim 255, wherein said nucleic acid product is single stranded. Claim 259 is drawn to the construct of claim 255, wherein said nucleic acid product is selected from the group consisting of antisense RNA, antisense DNA, sense RNA, sense DNA, a ribozyme, a protein binding nucleic acid sequence, and a combination of the foregoing.

De Young et al. taught making plasmid constructs as in figure 3 (page 12129) having U1-ribozyme constructs expressed from a T7 promoter. They taught on page 12130, col. 2, the expression of this construct in COS-1 cells. Since U1 introns are introns that are the same U1 introns used in the examples in the instant specification, and since the ribozymes taught by DeYoung et al. are flanked by the U1 intron in the same manner as the U1 intron flanks the

antisense in the examples in the instant specification, the U1 ribozyme constructs are considered to anticipate the instant claims.

10. Claims 255 and 258-260 are rejected under 35 U.S.C. 102(e) as being anticipated by Meyer, Jr. et al. (U.S. Patent 5,574,142).

Claim 255 is drawn to a nucleic acid construct which when introduced into a cell produces a nucleic acid product comprising a non-native processing element, which when in a compatible cell, said processing element is substantially removed during processing. Claim 258 states that the nucleic acid product is single stranded. Claim 259 states that the nucleic acid product is selected from antisense RNA, antisense DNA, sense RNA, sense DNA, a ribozyme and a protein binding nucleic acid sequence, or a combination of the foregoing. Claim 260 states wherein the protein binding nucleic acid sequence comprises a decoy that binds a protein required for viral assembly or viral replication.

Meyer, Jr. et al. taught a covalently lined conjugate of an oligonucleotide (ODN) with a peptide and a carrier or targeting ligand, where the oligonucleotide is capable of binding to a target sequence of DNA, RNA or protein inside the target cell. The peptide is capable of being digested by proteolytic enzymes inside the target cell and is thus a processing element that is substantially removed during processing. (See abstract and Figure 2) In col. 1, lines 16-34, they discuss where the ODN is an antisense oligonucleotide. In col. 2, lines 8-15, they discuss where the ODN is a ribozyme. In col. 1, line 53, through col.2 line 7, they discuss where the ODN

binds a protein, and wherein it binds HIV, and viral reverse transcriptase (required for viral replication). These ODNs are single stranded.

11. Claim 248 is considered free of the prior art since the closest prior art did not teach nor fairly suggest use of a primer comprising tRNA in a construct having a recognition site complementary to a primer for a non-native polymerase. The closest prior art for using a tRNA was in Rossi et al. (U.S. Patent 5,827,935) which taught in Figure 1 that a ribozyme coupled to a tRNA-Lys is useful for binding the HIV-1 mRNA transcript having a tRNA-Lys binding site for cleavage of the target HIV-1 mRNA molecule. However, they did not teach nor fairly suggest use of the tRNA primer in a construct for expressing a non-native polymerase, such as the HIV reverse transcriptase. Furthermore, Wagner et al. cited above did not teach nor fairly suggest use of a tRNA primer in their "autogene" constructs for gene expression from bacteriophage or mitochondrial non-native polymerases.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
April 5, 2003

JOHN L. LEGUYADER
SUPERVISORY PATENT EXAMINER
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